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TITLE: Phospholipase A.sub.2 inhibition using
4,1-benzoxazepine-2-(3H)-ones

BSPR:

Some examples of direct phospholipase A.sub.2 inhibition are known. Indomethacin, a drug with anti-inflammatory properties, has been shown to inhibit at least one phospholipase A.sub.2 enzyme. See K. L. Kaplan, et al., Proc. Natl. Acad. Sci., Vol. 75, No. 6, pp. 2955-2988 (1978). The compound has been shown to inhibit phospholipase A.sub.2 enzymes, isolated respectively from the venoms of Russel Viper, Crotalus adamanteus, and bee, and from pig pancreas. Certain local anesthetics have been shown to inhibit phospholipase A.sub.2 activity by competing with calcium ion, which appears to be a requirement for phospholipase activity. See W. Vogt, Advances in Prostaglandin and Thromboxane Research, Vol. 3 p. 89 (1978). Bromphenacyl bromide has been shown to inhibit phospholipase A.sub.2 by acylating a histadine residue which is the active site of the molecule. See M. Roberts, et al., Journal of Biological Chemistry, Vol. 252, pp. 2405-2411 (1977). R. Blackwell, et al., in British Journal of Pharmacy, Vol. 62, p. 79-89 (1978) has disclosed that mepacrine inhibits the activity of phospholipase A.sub.2 derived from perfused guinea pig lung. Certain butyrophenones are disclosed as phospholipase A.sub.2 inhibitors in U.S. Pat. No. 4,239,780.